

Claims

1. A system for shunting cerebrospinal fluids from a brain ventricle to the sinus system of an individual, said system comprising
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- i) a shunt body allowing fluid communication between a brain ventricle and a part of the sinus system of the individual,
- wherein said shunt body comprises a flow restricting component capable of maintaining a passive and essentially constant resistance to flow of cerebrospinal fluids through the shunt body,
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- ii) a brain ventricle catheter connected to the shunt body at a first location thereof,
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- wherein the brain ventricle catheter is capable of draining cerebrospinal fluids from a brain ventricle to the shunt body, and
- iii) a sinus catheter connected to the shunt body at a second location thereof,
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- wherein the sinus catheter is capable of draining, to the sinus system of the individual, cerebrospinal fluids having been drained from the brain ventricle and passed through the flow restricting component of the shunt body to the sinus catheter,
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- wherein i) the internal or external surface of the shunt body, or ii) the internal or external surface of the brain ventricle catheter, or iii) the internal or external surface of the sinus catheter, comprises a biocompatible and/or hemocompatible material comprising an inert surface preventing biological material from maintaining longer lasting contact with the inert surface, wherein said hemocompatible material is preferably coated with a plurality of charged species capable of increasing the hemocompatibility of the surface.
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2. The shunt system for shunting cerebrospinal fluids according to claim 1, wherein the flow restricting component is capable of maintaining a resistance to flow of cerebrospinal fluids of a constant value of from 0.1 to less than 8 mm Hg/ml/min.
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3. The shunt system for shunting cerebrospinal fluids according to claim 1, wherein the flow restricting component is capable of maintaining a passive resistance to flow of cerebrospinal fluids of a constant value of from 0.5 to less than 8 mm Hg/ml/min.
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4. The shunt system for shunting cerebrospinal fluids according to claim 1, wherein the flow restricting component is capable of maintaining a passive resistance to flow of cerebrospinal fluids of a constant value of from 1 to less than 8 mm Hg/ml/min.
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5. The shunt system for shunting cerebrospinal fluids according to claim 1, wherein the flow restricting component is capable of maintaining a passive resistance to flow of cerebrospinal fluids of a constant value of from 2 to less than 8 mm Hg/ml/min.
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6. The shunt system for shunting cerebrospinal fluids according to claim 1, wherein the flow restricting component is capable of maintaining a passive resistance to flow of cerebrospinal fluids of a constant value of from 3 to less than 8 mm Hg/ml/min.
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7. The shunt system for shunting cerebrospinal fluids according to claim 1, wherein the flow restricting component is capable of maintaining a passive resistance to flow of cerebrospinal fluids of a constant value of from 4 to less than 8 mm Hg/ml/min.
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8. The shunt system for shunting cerebrospinal fluids according to claim 1, wherein the flow restricting component is capable of maintaining a passive resistance to flow of cerebrospinal fluids of a constant value of from 6 to less than 8 mm Hg/ml/min.

9. The shunt system for shunting cerebrospinal fluids according to claim 1, wherein the flow restricting component is capable of maintaining a passive resistance to flow of cerebrospinal fluids of a constant value of from 0.1 to 7 mm Hg/ml/min.
- 5 10. The shunt system for shunting cerebrospinal fluids according to claim 1, wherein the flow restricting component is capable of maintaining a passive resistance to flow of cerebrospinal fluids of a constant value of from 0.1 to 6 mm Hg/ml/min.
- 10 11. The shunt system for shunting cerebrospinal fluids according to claim 1, wherein the flow restricting component is capable of maintaining a passive resistance to flow of cerebrospinal fluids of a constant value of from 0.1 to 5 mm Hg/ml/min.
- 15 12. The shunt system for shunting cerebrospinal fluids according to claim 1, wherein the flow restricting component is capable of maintaining a passive resistance to flow of cerebrospinal fluids of a constant value of from 0.1 to 4 mm Hg/ml/min.
- 20 13. The shunt system for shunting cerebrospinal fluids according to claim 1, wherein the flow restricting component is capable of maintaining a passive resistance to flow of cerebrospinal fluids of a constant value of from 0.1 to 3 mm Hg/ml/min.
- 25 14. The shunt system for shunting cerebrospinal fluids according to claim 1, wherein the flow restricting component is capable of maintaining a passive resistance to flow of cerebrospinal fluids of a constant value of from 0.1 to 2 mm Hg/ml/min.
- 30 15. The shunt system for shunting cerebrospinal fluids according to claim 1, wherein the flow restricting component is capable of maintaining a passive resistance to flow of cerebrospinal fluids of a constant value of from 0.1 to 1 mm Hg/ml/min.
- 35 16. The shunt system for shunting cerebrospinal fluids according to claim 1, wherein the flow restricting component is capable of maintaining a passive resistance to flow of cerebrospinal fluids of a constant value of from 1 to 7 mm Hg/ml/min.
17. The shunt system for shunting cerebrospinal fluids according to claim 1, wherein the flow restricting component is capable of maintaining a passive resistance to flow of cerebrospinal fluids of a constant value of from 1 to 5 mm Hg/ml/min.

18. The shunt system for shunting cerebrospinal fluids according to claim 1, wherein the flow restricting component is capable of maintaining a passive resistance to flow of cerebrospinal fluids of a constant value of from 1 to 3 mm Hg/ml/min.
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19. The shunt system for shunting cerebrospinal fluids according to claim 1, wherein the flow restricting component is capable of maintaining a passive resistance to flow of cerebrospinal fluids of a constant value of from 1 to 2 mm Hg/ml/min.
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20. The shunt system for shunting cerebrospinal fluids according to claim 1, wherein the flow restricting component is capable of maintaining a passive resistance to flow of cerebrospinal fluids of a constant value of from 2 to 7 mm Hg/ml/min.
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21. The shunt system for shunting cerebrospinal fluids according to claim 1, wherein the flow restricting component is capable of maintaining a passive resistance to flow of cerebrospinal fluids of a constant value of from 2 to 6 mm Hg/ml/min.
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22. The shunt system for shunting cerebrospinal fluids according to claim 1, wherein the flow restricting component is capable of maintaining a passive resistance to flow of cerebrospinal fluids of a constant value of from 2 to 5 mm Hg/ml/min.
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23. The shunt system for shunting cerebrospinal fluids according to claim 1, wherein the flow restricting component is capable of maintaining a passive resistance to flow of cerebrospinal fluids of a constant value of from 1 to 4 mm Hg/ml/min.
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24. The shunt system for shunting cerebrospinal fluids according to claim 1, wherein the flow restricting component is capable of maintaining a passive resistance to flow of cerebrospinal fluids of a constant value of from 4 to less than 8 mm Hg/ml/min.
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25. The shunt system for shunting cerebrospinal fluids according to claim 1, wherein the flow restricting component is capable of maintaining a passive resistance to flow of cerebrospinal fluids of a constant value of from 0.1 to 0.5 mm Hg/ml/min, such as from 0.5 to 1.0 mm Hg/ml/min, for example from 1.0 to 1.5 mm Hg/ml/min, such as from 1.5 to 2.0 mm Hg/ml/min, for example from 2.0 to 2.5

- mm Hg/ml/min, such as from 2.5 to 3.0 mm Hg/ml/min, for example from 3.0 to 3.5 mm Hg/ml/min, such as from 3.5 to 4.0 mm Hg/ml/min, for example from 4.0 to 4.5 mm Hg/ml/min, such as from 4.5 to 5.0 mm Hg/ml/min, for example from 5.0 to 5.5 mm Hg/ml/min, such as from 5.5 to 6.0 mm Hg/ml/min, for example from 6.0 to 6.5 mm Hg/ml/min, such as from 6.5 to 7.0 mm Hg/ml/min, for example from 7.0 to 7.5 mm Hg/ml/min, such as from 7.5 to less than 8.0 mm Hg/ml/min, for example from 0.1 to 1 mm Hg/ml/min, such as from 1 to 2 mm Hg/ml/min, for example from 2 to 3 mm Hg/ml/min, such as from 3 to 4 mm Hg/ml/min, for example from 4 to 5 mm Hg/ml/min, such as from 5 to 6 mm Hg/ml/min, for example from 6 to 7 mm Hg/ml/min, such as from 7 to less than 8 mm Hg/ml/min, for example from 0.1 to 2 mm Hg/ml/min, such as from 2 to 4 mm Hg/ml/min, for example from 4 to 6 mm Hg/ml/min, such as from 6 to less than 8 mm Hg/ml/min, for example from 0.1 to 2.5 mm Hg/ml/min, such as from 2.5 to 5.0 mm Hg/ml/min, for example from 5.0 to 7.5 mm Hg/ml/min, such as from 3.0 to 7.0 mm Hg/ml/min, for example from 3.5 to 6.5 mm Hg/ml/min, such as from 4.0 to 6.0 mm Hg/ml/min, for example from 4.5 to 5.5 mm Hg/ml/min, such as about 5.0 mm Hg/ml/min.
26. The shunt system according to any of claims 1 to 25 wherein the flow restricting component is selected from the group consisting of a tubular structure, a plurality of tubular structures, a porous mass, a fibrous mass, a structure being restricted by co-extending fibres arranged therein, and a structure being restricted by co-extending rods arranged therein.
27. The shunt system according to any of claims 1 to 25 wherein the flow restricting component comprises at least one tubular structure having an internal radius of more than 0.05 mm and preferably less than 0.50 mm, for example a tubular structure having an internal radius of about 0.06 mm, for example about 0.07 mm, such as about 0.08 mm, for example about 0.09 mm, such as about 0.10 mm, for example about 0.11 mm, such as about 0.12 mm, for example about 0.13 mm, such as about 0.14 mm, for example about 0.15 mm, such as about 0.16 mm, for example about 0.17 mm, such as about 0.18 mm, for example about 0.19 mm, such as about 0.20 mm, for example about 0.21 mm, such as about 0.22 mm, for example about 0.23 mm, such as 0.24 mm, for example 0.25 mm, such as 0.26 mm, for example 0.27 mm, for example about 0.28 mm, such

as about 0.29 mm, for example about 0.30 mm, such as 0.31 mm, for example 0.32 mm, such as 0.33 mm, for example 0.34 mm, for example about 0.35 mm, such as about 0.36 mm, for example about 0.37 mm, such as 0.38 mm, for example 0.39 mm, such as 0.40 mm, for example 0.42 mm, for example about 0.44 mm, such as about 0.46 mm, for example a tubular structure having an internal radius of about 0.48 mm.

28. The shunt system according to any of claims 26 and 27, wherein the flow restricting component comprises a single tubular structure having an internal diameter of less than 0.2 mm.

29. The shunt system according to any of claims 26 to 28, wherein the length of the at least one tubular structure is in the range of from about 3.0 mm to about 90 mm, such as from about 3.0 mm to about 80 mm, for example from about 3.0 mm to about 75 mm, such as from about 3.0 mm to about 70 mm, for example from about 3.0 mm to about 65 mm, such as from about 3.0 mm to about 60 mm, for example from about 3.0 mm to about 55 mm, such as from about 3.0 mm to about 50 mm, for example from about 3.0 mm to about 45 mm, such as from about 3.0 mm to about 40 mm, for example from about 3.0 mm to about 35 mm, such as from about 3.0 mm to about 30 mm, for example from about 3.0 mm to about 25 mm, such as from about 3.0 mm to about 22 mm, for example from about 3.0 mm to about 20 mm, such as from about 3.0 mm to about 18 mm, for example from about 3.0 mm to about 16 mm, such as from about 3.0 mm to about 14 mm, for example from about 3.0 mm to about 12 mm, such as from about 3.0 mm to about 10 mm, for example from about 10 mm to about 90 mm, such as from about 10 mm to about 80 mm, for example from about 10 mm to about 75 mm, such as from about 10 mm to about 70 mm, for example from about 10 mm to about 65 mm, such as from about 10 mm to about 60 mm, for example from about 10 mm to about 55 mm, such as from about 10 mm to about 50 mm, for example from about 10 mm to about 45 mm, such as from about 10 mm to about 40 mm, for example from about 10 mm to about 35 mm, such as from about 10 mm to about 30 mm, for example from about 10 mm to about 25 mm, such as from about 10 mm to about 20 mm, for example from about 10 mm to about 15 mm, such as about 10 mm, for example about 15 mm, such as about 20 mm, for example about 22 mm, such as about 24 mm, for example

about 26 mm, such as about 20 mm, for example about 22 mm, such as about 24 mm, for example about 26 mm, such as about 28 mm, for example about 30 mm, such as about 32 mm, for example about 34 mm, such as about 36 mm, for example about 38 mm, such as about 40 mm, for example about 45 mm, such as about 50 mm, for example about 55 mm, such as about 60 mm, for example about 65 mm, such as about 70 mm, for example about 75 mm, such as about 80 mm, for example about 85 mm.

30. The shunt system according to claim 29, wherein the total length of the at least one tubular structure is divided in two or more individual segments.

31. The shunt system according to any of claims 1 to 30 further comprising at least one check valve located within the shunt body for preventing cerebrospinal fluid from flowing back from the sinus catheter to the brain ventricle catheter.

32. The shunt system according to claim 31, wherein said at least one check valve does not have any inherent resistance or opening pressure and essentially does not exert any resistance on the flow of cerebrospinal fluid through the shunt body.

33. The shunt system according to claim 31 and 32, wherein the resistance to flow through the shunt body is independent of said at least one check valve and defined solely by the flow resistance of the flow restricting component.

34. The shunt system according to any of claims 31 to 33, wherein the operation of said at least one check valve is independent of a predetermined opening pressure to be overcome by the differential pressure defined by the difference between the intracranial pressure and the pressure in the sinus.

35. The shunt system according to any of claims 31 to 34, wherein said at least one check valve comprises a ball valve and optionally further comprises valve members selected from the group consisting of guided rigid valve members and flexible valve members, including rigid, ring shaped valve members, and flexible valve members such as tongue-shaped laminae.

36. The shunt system according to any of claims 31 to 35, wherein said at least one check valve comprises a mitral silicone valve.
37. The shunt system according to any of claims 1 to 36, wherein the brain ventricle catheter is connected to a first end location of said shunt body, and wherein said sinus catheter is connected to a second end location of said shunt body.
38. The shunt system according to any of claims 1 to 37 further comprising a shunt body (10) made from silicone rubber, an antechamber (11) having opposite flat walls (12) made from hard silicone rubber, and opposite domed walls (13) made from soft, perforatable, self-healing silicone rubber,
- wherein at the proximal end (the top end) the chamber walls end in a tapering end comprising a tip (14), to which a brain ventricle catheter (15) can be connected and secured,
- wherein the antechamber (11) is connected to the tubular flow restricting component (16) so that the distal end of the chamber (11) forms an inlet to a tubular flow restricting component (16),
- wherein a check valve or non-return valve (17) is arranged both at the entrance to the antechamber (11) and at the outlet of the tubular flow restricting component (16),
- wherein fluidic connection to the sinus system of the individual is provided by a tubular drain (18), and
- wherein fluidic connection to a brain ventricle of the individual is provided by a brain ventricle catheter (15).
39. The shunt system according to claim 38, wherein the brain ventricle catheter (15) is attached to the tip or inlet connector (14), which is provided with an annular bead, and wherein the brain ventricle catheter is optionally secured by means of a ligature.

40. The shunt system according to claim 39, wherein the length of the connector (14) is about 5 mm.
41. The shunt system according to any of claims 38 to 40, wherein the tubular flow restricting component (16) is dimensioned in accordance with Hagen-Poiseuille's law so as to provide a passive and substantially constant resistance to flow of less than 8 mm Hg/ml/min.
42. The shunt system according to any of claims 38 to 41, wherein the tubular flow restricting component is substantially straight, and/or wherein the inner walls of the flow restricting component are substantially smooth.
43. The shunt system according to any of claims 38 to 42, wherein the material from which the walls of the tubular flow restricting component is made is selected from the group consisting of hard silicone rubber, HD polyethylene, such as gas sterilized polypropylene, polycarbonate, polysulfone, polystyrene, PVC and titanium, vanadium steels, shape memory alloys such as Nitinol, aluminium, stainless steels, teflon, silastic, polyethylene, titanium alloys, and ultra-high molecular weight polyethylene/metal combinations.
44. The shunt system according to any of claims 38 to 43, wherein the tubular drain (18) for the sagittal sinus is made from titanium or silicone rubber.
45. The shunt system according to any of claims 38 to 44, wherein the distal 5 mm of the tubular drain (18) has an outer diameter of 2 mm and an inner diameter of 1.5 mm, and wherein the part of the drain that goes through the skull has generally an outer diameter of 3 mm and an inner diameter of 1.5 mm, and wherein the distance of the part of the drain with the largest diameter can be regulated so as to fit the distance from the shunt body to the hole over the sagittal sinus.
46. The shunt system according to any of claims 38 to 44, wherein the tubular drain (18) comprises a titanium tube with an inner diameter of 1.5 mm and a length of about 20 mm attached to a silicone rubber tube with an outer/inner diameter of 3/1.5 mm, and a length of about 60 mm.

47. The shunt system of claim 46, wherein the tubular drain (18) further comprises a stilet for guiding the silicone rubber tube into the sinus through a borehole in the skull of the individual.

5 48. A method for implanting different catheters of a cerebrospinal fluid shunt system into a brain ventricle and the sinus system, respectively, of an individual, said method comprising the steps of

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- i) providing a shunt system according to any of claims 1 to 47,
 - ii) placing the shunt body of the shunt system subcutaneously on top of the calvarium of an individual, optionally behind the coronal suture on one side of the sagittal suture,
 - 15 iii) inserting a second end of the brain ventricle catheter in a brain ventricle via a first borehole,
 - iv) optionally connecting a first end of the brain ventricle catheter to a first location on the shunt body;
 - 20 v) inserting a second end of the sinus catheter into the sinus system of the individual via a second borehole,
 - vi) optionally connecting a first end of the sinus catheter to a second loca-
25 tion on the shunt body,

wherein the shunt body provides fluidic communication between the brain ventricle catheter and the sinus catheter.

30 49. The method of claim 48, wherein the second end of the sinus catheter is inserted via the second borehole into one of the two large venous sinuses of the cranium that begin at the bony protuberance on the middle of the inner surface of the occipital bone at the intersection of its bony ridges and terminate at the jugular foramen on either side.

50. The method of claim 48, wherein the second end of the sinus catheter is inserted into the sagittal sinus via the second borehole.
51. The method of claim 48, wherein the second end of the sinus catheter is inserted into the transverse sinus via the second borehole.
52. The method of claim 48, wherein the second end of the brain ventricle catheter is inserted into the right brain ventricle via the first borehole.
53. The method of claim 48, wherein the second end of the brain ventricle catheter is inserted into the left brain ventricle via the first borehole.
54. The method of any of claims 48 to 53 comprising the further step of shunting cerebrospinal fluid from a brain ventricle and to either one or both of the two large venous sinuses of the cranium that begin at the bony protuberance on the middle of the inner surface of the occipital bone at the intersection of its bony ridges and terminate at the jugular foramen on either side.
55. The method of claim 54, wherein the cerebrospinal fluid is shunted from the brain ventricle and to the sagittal sinus.
56. The method of claim 54, wherein the cerebrospinal fluid is shunted from the brain ventricle and to the transverse sinus.
57. The method of any of claims 54 to 56, wherein the resistance to flow through the flow restricting component of the shunt body is from 2 to less than 8 mm Hg/ml/min.
58. The method of claim 57, wherein the resistance to flow through the flow restricting component of the shunt body is from 4 to 6 mm Hg/ml/min.
59. The method of claim 57, wherein the resistance to flow through the flow restricting component of the shunt body is about 5 mm Hg/ml/min.

60. A method for shunting cerebrospinal fluid from a brain ventricle to the sinus system of an individual, said method comprising the steps of

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- i) providing a shunt system according to any of claims 1 to 47,
 - ii) inserting the first catheter into a brain ventricle of the individual to drain cerebrospinal fluid from the brain ventricle,
 - 10 iii) inserting the second catheter into the sinus system of the individual to feed the cerebrospinal fluid via the shunt body into the sinus system,
 - iv) shunting cerebrospinal fluid from a brain ventricle to the sinus system of an individual
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- wherein the shunt member providing fluidic communication between the first and second catheters,

61. The method of claim 60, wherein cerebrospinal fluid is shunted from a brain ventricle and to either one or both of the two large venous sinuses of the cranium that begin at the bony protuberance on the middle of the inner surface of the occipital bone at the intersection of its bony ridges and terminate at the jugular foramen on either side.

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62. The method of any of claims 60 and 61, wherein the cerebrospinal fluid is shunted from the brain ventricle and to the sagittal sinus.

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63. The method of any of claims 60 and 61, wherein the cerebrospinal fluid is shunted from the brain ventricle and to the transverse sinus.

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64. The method of any of claims 60 to 63, wherein the resistance to flow through the flow restricting component of the shunt body is from 2 to less than 8 mm Hg/ml/min.

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65. The method of any of claims 60 to 63, wherein the resistance to flow through the flow restricting component of the shunt body is from 4 to 6 mm Hg/ml/min.

66. The method of any of claims 60 to 63, wherein the resistance to flow through the flow restricting component of the shunt body is about 5 mm Hg/ml/min.
- 5 67. The method of any of claims 60 to 66 for shunting cerebrospinal fluid, said method comprising the further step of preventing cerebrospinal fluid from flowing back from the second catheter to the first catheter by introducing at least one check valve into the shunt body.
- 10 68. The method of any of claims 60 to 67 for shunting cerebrospinal fluid, wherein the cerebrospinal fluid is shunted through at least one flow passage structure having an internal radius of about 0.20 mm.
- 15 69. The method of any of claims 60 to 68 for shunting cerebrospinal fluid, wherein the flow rate of shunted cerebrospinal fluid is constant.
70. The method of any of claims 60 to 69 for shunting cerebrospinal fluid, wherein the constant flow rate is in the range of from 40 ml per hour to 140 ml per hour.
- 20 71. The method of claim 70 for shunting cerebrospinal fluid, wherein the constant flow rate is about 40 ml per hour, such as about 45 ml/hour, for example 50 ml per hour, such as about 55 ml/hour, for example about 60 ml per hour, such as about 65 ml/hour, for example about 70 ml per hour, such as about 75 ml/hour, for example about 80 ml per hour, such as about 85 ml/hour, for example about 90 ml per hour, such as about 95 ml/hour, for example 100 ml per hour, such as about 105 ml/hour, for example about 110 ml per hour, such as about 115 ml/hour, for example about 120 ml per hour, such as about 125 ml/hour, for example about 130 ml per hour, such as about 135 ml/hour, for example about 140 ml per hour, such as from 40 to 50 ml per hour, for example from 50 to 60 ml per hour, such as from 60 to 70 ml per hour, for example from 70 to 80 ml per hour, such as from 80 to 90 ml per hour, for example from 90 to 100 ml per hour, such as from 110 to 120 ml per hour, for example from 120 to 130 ml per hour, such as from 130 to 140 ml per hour.
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72. The method of any of claims 60 to 71 for shunting cerebrospinal fluid, wherein the intracranial pressure of the individual is in the range of from -170 mm Hg to 200 mm Hg.
- 5 73. The shunt of any of claims 1 to 47, wherein said biocompatible and/or hemocompatible material is carbon-based.
74. The shunt of claim 73, wherein said biocompatible and/or hemocompatible material comprises or consists of Diamond-Like Carbon (DLC).
- 10 75. The shunt of claims 73, wherein said biocompatible and/or hemocompatible material comprises or consists of a turbostratic carbon.
76. The shunt of claim 75, wherein said biocompatible and/or hemocompatible material comprises or consists of pyrolytic carbon.
- 15 77. The shunt of any of claims 1 to 47, wherein said biocompatible and/or hemocompatible material comprises or consists of a Sputtered carbon.
- 20 78. The shunt of claim 77, wherein said biocompatible and/or hemocompatible material comprises or consists of Graphit-iC.
79. The shunt of any of claims 1 to 47, wherein said biocompatible and/or hemocompatible material comprises or consists of Teflon and the like.
- 25 80. The shunt of any of claims 1 to 47, wherein said biocompatible and/or hemocompatible material comprises or consists of a Ceramic.
81. The shunt of claim 80, wherein said biocompatible and/or hemocompatible material comprises or consists of titanium nitride (TiN).
- 30 82. The shunt of any of claims 1 to 47, wherein said biocompatible and/or hemocompatible material comprises or consists of Phosphatidyl choline di-ester.

83. Use of a shunt body comprising a flow restricting component capable of maintaining a passive and essentially constant resistance to outflow of CSF through the shunt body, in the manufacture of a shunt system according to any of claims 1-47 and 73-81, for the treatment of an individual suffering from, or at risk of developing, a condition related to the retention and/or accumulation of toxic substances in brain tissue and/or the CSF space.

84. The use according to claim 83, wherein said condition is Alzheimer's disease.

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